UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
09/070,629	04/30/98	PALESE	P 6923-071-999

EXAMINER

HM12/0524

PENNIE & EDMONDS
1155 AVENUE OF THE AMERICAS
NEW YORK NY 10036-2711

ART UNIT | PAPER NUMBER
1641 | 12

DATE MAILED: 05/24/00

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 2/18/00

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-19 is/are pending in the application.

Of the above, claim(s) 12-19 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-11 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of Reference Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

– SEE OFFICE ACTION ON THE FOLLOWING PAGES –

PTOL-326 (Rev. 10/95)

★ U.S. GPO: 1996-410-238/40050

Claims 1-19 are pending in this application. Claims 12-19 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 11.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 8 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 8 is limited to a killed virus and is therefore improper since it is ultimately dependent from a claim which requires that the virus be attenuated. Thus, the claim fails to further limit since by definition a killed virus cannot merely be attenuated.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

Claims 1-11 rejected under 35 U.S.C. 102(e) as being anticipated by Palese et al (5,578,473).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived

from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Palese et al. (U.S. Patent 5,578,473) teach that which is broadly claimed. Instant claim limitations are clearly addressed by the patent as set forth below. That is, Palese et al. clearly teach recombinant negative strand virus RNA templates which may be used to express heterologous gene products and/or to construct chimeric viruses. The reference teaches that the negative-strand viruses such as influenza would be attractive candidates for constructing chimeric viruses for use in vaccines because genetic variability allows for the construction of a vast repertoire of vaccine formulations which will stimulate immunity without risk of developing a tolerance. However, achieving this goal has been precluded by the fact that, to date, it has not been possible to construct recombinant or chimeric negative-strand RNA particles that are infectious. Although the influenza virus genome consists of eight functional gene segments it is unknown how many actual segments a virus packages. It has been suggested that influenza can package more than eight segments, and possibly up to 12. This would allow for easier propagation of recombinant virus in that the "ninth" gene segment could be designed to express the foreign gene product. Although this "ninth" segment may be incorporated into some viruses, it would soon be lost during virus growth unless some selection is supplied. This can be accomplished by "uncoupling" the NS or M gene segment. The NS2 coding portion could be removed from the NS gene segment and placed on the gene segment coding for the foreign protein (along with appropriate splicing signals). Alternatively, a bicistronic mRNA could be constructed to permit internal initiation to "unsplice" these viral sequences. The resulting recombinant virus with the "uncoupled" NS or M gene would be able to propagate on its own and

also would necessarily have to package the "ninth" gene segment, thus ensuring expression of the foreign gene. An mRNA may be packaged in vivo by cloning the gene of interest, such as the CEA gene (TAA) (associated with many different tumors and thought to be a tumor rejection antigen), into a vector such as pAR-1. The gene would be cloned immediately downstream of the operator sequence in pAR-1. The EMCV translation sequence would be cloned between the operator and the CEA coding sequence. In this way, the CEA RNA may be translated without requiring a 5' CAP to enhance translation of the mRNA. Insertion of the heterologous gene sequence into the HA or NA gene segments. An intact HA molecule with a substitution only in antigenic sites may allow for HA function and thus allow for the construction of a viable virus. Therefore, this virus can be grown without the need for additional helper functions. Of course, the virus should be attenuated in other ways to avoid any danger of accidental escape. Either a live recombinant viral vaccine or an inactivated recombinant viral vaccine can be formulated. A live vaccine may be preferred because multiplication in the host leads to a prolonged stimulus of similar kind and magnitude to that occurring in natural infections, and therefore, confers substantial, long-lasting immunity. Production of such live recombinant virus vaccine formulations may be accomplished using conventional methods involving propagation of the virus in cell culture or in the allantois of the chick embryo followed by purification. Such preparations may transcribe and translate--in this abortive cycle--a sufficient number of genes to induce an immune response. Alternatively, larger quantities of the strains could be administered, so that these preparations serve as inactivated (killed) virus vaccines.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laurie Scheiner, whose telephone number is (703) 308-1122. Any inquiry

of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703) 308-0196.

Correspondence related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Official communications should be directed toward one of the following Group 1600 fax numbers: (703) 308-4242 or (703) 305-3014. Informal communications may be submitted directly to the Examiner through the following fax number: (703) 308-4426. Applicants are encouraged to notify the Examiner prior to the submission of such documents to facilitate their expeditious processing and entry.

Laurie Scheiner/LAS
May 12, 2000

LAURIE SCHEINER
PRIMARY EXAMINER